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THE DIAGNOSIS OF INTRAOCCULAR TUMORS; A DEMONSTRATION OF KODACHROME SLIDES

ARTHUR J. BEDELL, M. D.,
Albany, New York

The exposition considered retinoblastoma, metastatic carcinoma of the choroid, malignant melanoma, and a meningioma. A short history of each case was presented and the disease described in detail. Congenital retinal pigmentation, benign melanoma, angiomas of retinae, angioma, and choroidal hemorrhage were shown and the differential diagnosis explained.

Retinoblastoma, the glioma of the textbooks, is a rapidly growing intraocular tumor seen in infancy and early childhood. The diagnosis is made when there is a yellow pupillary reflex, the history of progressive loss of vision and frequently a marked irritability of the nervous system. If the growth is extensive, gross vessels are visible on it. At other times pale yellow spots appear in the iris and a soft, yellow cellular mass in both the vitreous and the aqueous. This moves on motion of the globe and settles below like an ordinary hyphema. This is one of the most urgent of all eye diseases for if the diagnosis is delayed, the growth increases and may break through the globe, or extend along the optic nerve to the brain. The prognosis is very grave and enucleation must be performed promptly. Several reported cases suggest a familial predilection and under such conditions further pregnancy should be avoided.

In premature babies there is often an arrested dissolution of the vascular framework of the vitreous. This may at times give a yellow reflex to the pupil and looks like a retinoblastoma. However, a careful inspection will disclose a grayish tinge to the mass. The fetal remains may be complete producing a graying pupillary reflex, partial with smooth vascular remnants, or large waving folds. This

condition must be excluded in all babies before considering anything else.

Purulent infiltration of the vitreous may obviously give a yellow reflex or completely fill the vitreous. The history of injury or infection assists in the diagnosis.

These conditions were illustrated by ten original kodachromes; an eye with metastasis in the iris, rapidly growing, soft cellular mass in the vitreous, a growth completely filling the globe and forming a ring of tumor about the cornea; persistent hyaloid membrane in an eye which was enucleated because of glaucoma; and a purulent vitreous.

The next group were metastatic carcinomas of the choroid. Two cases were presented, in each the patient had had a breast removed for carcinoma.

The first eye symptom was blurred vision caused by a flat detachment of the retina. The pupil was larger in the more affected eye, later in the course of the disease there was a dull gray pupillary reflex and the slightly elevated detached retina was seen.

In both patients glaucoma developed and the affected eyes were removed. The condition may follow carcinomas in other sites but it is very unusual. The disease is rare, only 250 cases are recorded. It is another disease the diagnostician must remember, for when the patient who has had a carcinoma of the breast complains of failing vision, metastasis must be excluded. When the eye is painless, enucleation is not advised for the general body metastasis is fatal. The patient usually lives only a short time after the eye becomes involved.

Malignant melanomas, commonly called sarcoma of the choroid, made up the last and largest group. The alleged onset of this disease is as variable as the disposition of the individual. A patient said her vision was perfect until two days before her eye was removed for a large, mushroom-shaped, densely pigmented choroidal tumor, which had obviously

been present for months. The tumor may become so large that it breaks through the sclera and the patient seeks relief from the annoying bleeding. The time relief is sought depends upon the primary site of the tumor. When it is central, patients come early because of a blind spot. The growth may be very small and call for great skill in correctly diagnosing it. Or the first symptom the patient notices may be a sudden, complete blindness, which examination discloses to be a detachment of the retina. It is often difficult to diagnose a tumor as the cause of the detachment. The detachment may look like an ordinary fluid separation of the retina, or it may be attached to the growth. I have found that a careful history of the onset of the blindness is often of great value and that an accurate field for light projection is a very important factor in determining the cause of the separation. If the growth is in the anterior portion of the globe, transillumination is of great help, but when it is at the posterior pole, this method is less applicable or even impossible.

Twenty kodachromes were exhibited to show the tumors ranging from a small, flat central tumor to one half filling the globe and detachments from one localized to the tumor, to a complete separation of the retina. A case of local orbital recurrence was explained and another of metastasis with generalized carcinomatosis. It is well to remember that when a patient presents with abdominal symptoms after an enucleation liver metastasis must be excluded, thus preventing a number of unnecessary operations.

Whenever a patient complains of poor vision, an expert ophthalmoscopic examination is imperative for the background of the eye is the stage on which not only malignancies but practically all of the constitutional diseases known to man may make their original appearance.

One case of meningioma causing a choked disc and proptosis was also shown.

The differential diagnosis of various closely allied symptom complexes is the most interesting of medical problems and calls for an ever widening field of observation. Before an eye is removed all measures should be employed to exclude benign tumors and other diseases.

As an example, a patient came in with a diagnosis of intraocular tumor and said she had been advised to have the eye enucleated. The sclerosis of the retinal arteries and veins and areas of exudate were sufficient to make the diagnosis of sarcoma questionable and choroidal hemorrhage probable. Several fundus pictures were shown to prove the diagnosis and illustrate how the blood was absorbed.

In the degeneration of the macular choroid and retina of the elderly, a central mass may suggest a tumor but observation over a long time and attention to the general circulatory symptoms will be sufficient to save many eyeballs from the hands of an operator.

Among the other confusing conditions is a round, macular retinochoroiditis which may suggest a tumor. It is circumscribed, elevated 1 to 2 diopters and frequently has a finely pigmented surface. It is benign and no operation is indicated.

In tuberculous choroiditis massive exudates sometimes suggest malignant growths, but a careful history and examination will prevent errors.

The photographs of an angiomas retinæ showed the very large veins and arteries extending to an oval somewhat nodular mass. This interesting condition does not warrant enucleation for it is often part of a general vascular disease with angiomas in many parts of the body, such as the cerebellum.

Pigmentations may be isolated brown, subretinal or deep retinal spots over which the retinal vessels pass. They rarely enlarge and may be excluded from the malignant spots by careful re-examinations. The malignant melanomas usually show appreciable and measurable growth in three or four weeks and there is often a secondary tumor in the same eye. This was shown by photographs where the benign growth remained unchanged for years and in the malignant where an increase in the size of the tumor was marked in one month.

The other confusing pigmentation is the congenital, where there are usually several stationary brown spots in a sector of the fundus. The larger areas are always the more peripheral.

SUMMARY

The usual intraocular malignancies were exhibited by 90 kodachrome slides.

Some points of differentiation were illustrated.

The object of the demonstration was to make all more conscious of intraocular malignancies.

DISCUSSION

DR. W. O. LAMOTTE (Wilmington): Mr. President, members of the Society and guests. It is an honor to open the discussion on a paper by Dr. Bedell, who has spoken pretty much all over the country. I feel something like Dr. Beech said he felt when he was lecturing on optics, with Dr. Lancaster sitting in the audience.

February 29, 1928, Mrs. T., age 27 years, was seen because of a blind left eye which occurred in 1927 during pregnancy. Vision was light perception. She was using drops in this eye, prescribed by two different oculists at different times. There was a pigmented mass in contact with the posterior surface of the lower part of the lens. Transillumination over the lower part of the sclera gave no reflex; it did over the upper part. Tension was 40 (Schiotz). Diagnosis was pigmented sarcoma of the choroid. The eye was enucleated the day after the first visit. It was sectioned by a competent ocular pathologist. Half of the eye was returned with the sections to me but no malignancy had been found. The half in my possession was sent back to the pathologist to make sections of this part. These showed a spindle-celled partly pigmented sarcoma. The patient is living and well today.

A blind and phthisical eye frequently contains a tumor. Absolute glaucoma in which the fundus cannot be seen may contain a malignant tumor. In a study of 402 such cases by one author 10 per cent were found malignant.

I would like to ask Dr. Bedell, if he doesn't mind, what are the statistics on incidence of ultimate death by metastasis to other parts, and what is known about how early these metastases occur, for example, in a small melanoma as seen in a normal seeing eye? What would be your course of action? Is there any evidence that there is less metastasis from early removal than removal in later years?

DR. N. L. CUTLER (Wilmington): Dr. Bedell, Mr. Chairman, I won't take up any of your time. I possibly can't help but say that perhaps you appreciate that an ophthalmolo-

gist occasionally has something more confronting him than just a refraction. We have had the opportunity this afternoon to see some photographs both of the fundus and of the eye which are classics. I think I am stating a fact when I say that. There are certainly no better fundus photographs in the world than Dr. Bedell has, and there is no better technician and also student of fundus photographs than Dr. Bedell. I emphasize this because I know the men who are for the most part directly interested in ophthalmology, and his reputation is not nationwide, it is worldwide, and it has been a great privilege to hear Dr. Bedell.

He has stated that some patients went down the river. I think you will all agree with me that they would have been more fortunate in this case if they had gone up the river, reversing the usual opinions.

There are only one or two things that I would like to bring out; one of them is a question I would like to ask Dr. Bedell. I would like to ask Dr. Bedell how much importance he places on elevation in a benign, apparently benign melanoma of the choroid? This is a problem which probably confronts ophthalmologists more frequently than some of the other conditions which he has discussed. At the present time I just happen to have two cases which have elevation of the benign melanoma, apparently benign, one in a one-eyed patient. photographs, which were taken for me at the

I have a few slides here, kodachrome fundus University of California, which I hesitate to show after the pictures that have been shown here. However, they were taken at the University of California. One is supposed to be focused on the tumor and one on the retina. Standing at this distance I am not sure which is which. This was an optic nerve tumor occurring in a medical officer in his 30's who noticed about June of 1944, looking through field glasses, that the vision in one eye was not as good as the other. He finally found his way to our hospital in March of 1945, and we saw this pinkish yellow elevation on the optic nerve. He was seen by Dr. Cortez, Professor of Ophthalmology at the University of California.

The question came up as to whether this was a rather rare tumor known as a perifeloma. He took a leave and came East intending to see

some other men in consultation. He saw Dr. Dunnington in New York and he also saw Dr. Arnold Knapp. The consensus was that this was a malignancy and that the eye should be removed, which was done in due course. The slide was sent to the Army Medical Museum. Colonel Ash sent a report back to me that it was a glioma. The slide was also sent to Dr. Alvarez of New York at Columbia Presbyterian and his opinion was it was angioma epithelioma. The slide was also sent to Dr. Verhoff of Boston, another authority, and he agreed with Dr. Alvarez.

The result of the pathological examination indicated that we had removed an eye with a benign tumor. That is one of the problems, of course, one does face. Apparently there is just a little bit of room left by these men for a change in their minds.

I am wondering, if from these rather poor photographs, Dr. Bedell could give some further enlightenment upon these cases. This is going to be published by Dr. Silvers of Reading Hospital who happens to be here today and we have been interested in it.

Thank you very much for a very enjoyable presentation, Dr. Bedell.

DR. J. M. MESSICK (Wilmington): Dr. Bedell and gentlemen: Obviously this discussion belongs to the ophthalmologists, but I have been attending many medical meetings here and there, and I have passively heard a lot of talk on ocular conditions of one kind or another, but it has never been my privilege to hear and to see such a presentation. I am sure that those who see such exquisite photographs, certainly to those of us who are not ophthalmologists, this presentation brings home at least two points, one is that when we see unusual eye conditions this should persuade us to get to an ophthalmologist in a hurry; and secondly, emphasizes again the tremendous help we can get from the ophthalmologist if we only ask for it.

PRESIDENT W. C. DEAKYNE (Smyrna): Is there any further discussion? If not, I will ask Dr. Bedell to close the discussion.

DR. BEDELL: I will consider Dr. Cutler's question first. Dr. Cutler, there is a very distinct similarity in the contour of the mass you report and the angiomas which I presented. Your case is unique because the tumor is located on the disc and this prevented the forma-

tion of dilated vessels which are characteristic of the disease. If I had seen it, I would have advised delay, because by photographs the size of the lesion and its elevation could have been observed and prognosis be based on the photographic evidence. It is a very interesting case and I am very glad to have seen the photograph.

Dr. Cutler asks what significance I place on elevation. A benign melanoma lies beneath the retinal vessels, which pass over it usually uninterrupted in course or size. I have seen benign melanomas elevated about two-thirds of a millimeter, and they have remained for years without change. I do not believe it possible to always be sure of the diagnosis on one examination. It is my habit to examine and photograph repeatedly and if the area enlarges to consider the case as probably malignant especially if the growth becomes thicker as well as more extensive. I do not consider mere elevation of a dark patch an indication for the removal of the eye.

Dr. LaMotte asks about statistics on metastatic growth. I cannot answer his question. I have over 100 specimens of sarcoma of the choroid, and I am sure that both Dr. LaMotte and Dr. Cutler will agree that it is a large collection. Metastasis has not seemed to be dependent upon the size of the tumor, the time the eye was removed nor on the degree of pigmentation of the tumor. In other words, I can't tell why one metastasizes promptly and why the other goes on quietly for years. And for the same reason, I cannot answer some of the other questions regarding the source of light. It does not then, in my experience, depend upon the size of tumor, its location, or the degree of pigmentation.

Some years ago, I spoke on glaucoma and a man whom I knew to have a large and active medical practice said, "I never saw an acute glaucoma in my practice." I thought that was surprising. Within six weeks I operated on five of his glaucoma patients. This is stated to remind you that you must become conscious of entities such as intraocular malignancies.

I thank Dr. Messick for his gracious remarks.

It has been very pleasant to be with you. I have profited by the papers of the morning and have been delighted this afternoon.

HYALURONIDASE

O. J. POLLAK, M. D., Ph. D.,*

Wilmington, Del.

While only one spermatozoon actually unites with the ovum, millions of spermatozoa are necessary for impregnation. A sperm count of 60 millions per c. c. and of 300 millions per semen sample is generally accepted as a minimum for a man to be considered fertile. We know that men with a much lower sperm count may father a child; however, the ability to impregnate decreases rapidly with the drop in the number of spermatozoa. The phenomenon of polyspermia as a prerequisite for the union of the nuclei of the two gamets has attracted the attention of investigators for centuries.

In 1930 Yamane¹ sterilized male rabbits by vasectomy and compared ova washed out from the fallopian tube after copulation with these animals with ova from fertile copulation. He showed that ova from fertile cohabitation are much sooner devoid of corona cells than ova from non-fertile conjugation: At a time the corona of the non-fertilized ova just starts to break up, the fertilized ovum has reached the two-cell stage. The same was observed *in vitro*. In 1935 Pineus and Enzmann² realized that disintegration of the corona depends upon the number of spermatozoa and stated as minimum requirement for the process a count of 20 million spermatozoa per c. c.

In 1942 McClean and Rowlands³ construed a new fermentative-chemical theory of fertilization. They assumed that the seminal hyaluronidase attacks the intercellular substance of the corona radiata which surrounds the ovum in the fallopian tube. The spermatozoon cannot penetrate the ovum unless the corona radiata has been destroyed. By placing fresh ova of rats into extracts with hyaluronidase parallelism between the speed of disintegration of the corona and the concentration of the enzyme has been demonstrated. The enzyme is carried to the place of its action by spermatozoa and thus its amount in the fallopian tube depends upon the number of spermatozoa. A subnormal sperm count results in lack of hyaluronidase and subsequently in lowered fertility. Addition of the enzyme to suspensions of rabbits' spermatozoa seemed

to improve the results of artificial insemination.

Hyaluronidase activity has been observed in extracts of testicles with histologically proven spermatogenesis but not in extracts of gonads without a normal maturation of the germ cells. The observation that a latecomer among the spermatozoa penetrates the ovum rather than one of the spermatozoa which arrived first in the fallopian tube tends to support the fermentative-chemical theory.

Hyaluronidase is an enzyme which acts specifically upon hyaluronic acid. The enzyme and the acid are present in mesothelial mucus. Trypsin, pepsin and diastase either do not act upon mesothelial mucus at all, or to only a very slight degree. On the other hand, hyaluronidase is ineffective against mucus from salivary glands or from bronchi. Hyaluronidase is present in the extract of testicles, placenta, in the vitreous humor, umbilical cord, synovial and pleural fluid, in malignant tumors including sarcoma of fowl, snake and spider poisons, leeches, and in bacteria such as those of the malignant edema group. The enzyme seems to be present wherever there is destruction of normal tissues.

Hyaluronic acid conjugated with sulfuric acid is present in the interstitial substance of connective tissue. The protein-free fraction of mucus, obtained by salting-out or by tryptic digestion of the material, may be broken down into equimolar amounts of acetylglucosamine and glucuronic acid.

At present, hyaluronidase can be detected by several methods. Duran-Reynals⁴ inject an extract of the material to be tested together with a colored indicator into the skin of an experimental animal and compare its spread with the moderate spread of the indicator alone. The test is known as Reynolds' test, or the spreading or diffusion factor. Chain and Duthie⁵ observed that the viscosity of a mucoprotein solution decreases with an increased amount of mucinase. At the same time, reducing substances are being liberated. This method requires the preparation of a substrate. Umbilical cord may be used as basic material. After removal of all blood, the cord is hashed, extracted with water, the mucin precipitated with alcohol acidified with acetic

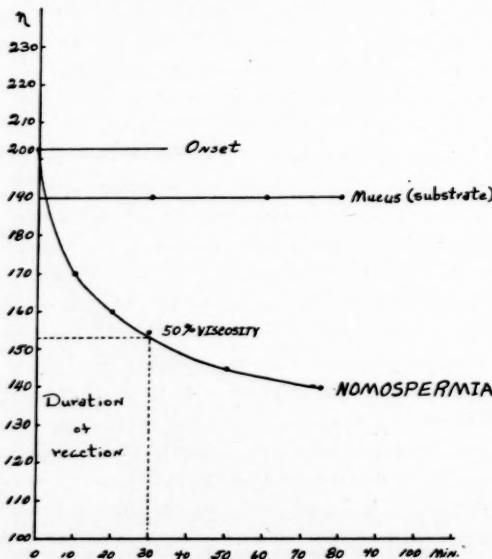
* Pathologist, Wilmington General Hospital.

acid, desiccated in a vacuum over calcium chloride, and finally powdered. The light powder is soluble in water and in physiologic saline solution. Meyer and Palmer⁶ identified such substrate as a glucoprotein similar to mucoidinsulphuric acid or chondroitinsulphuric acid.

A complete semen analyses shall in the future include an assay of hyaluronidase. Preparation of a suitable substrate is fairly simple but the enzyme which is needed for control purpose is not yet readily available. In practice, hyaluronidase in semen is best measured with the aid of a viscosimeter. The viscosity of a solution of the substrate is adjusted so that it is three times that of distilled water. A 0.3 per cent solution usually has this property. Of such solution 5.0 c. c. are drawn into the lower bulb of an Ostwald viscosimeter and then 0.5 c. c. of fresh semen. The content is mixed and, with the aid of a rubber balloon, is drawn into the upper bulb until the meniscus reaches the upper mark of the apparatus. Then the material is allowed to flow from the upper to the lower mark.

The following readings and calculations are made:

- The time at onset of flow is recorded
- The time of flow of the semen-mucus mixture from one mark to the other is timed with a stop-watch



Graph I: VISCOSITY OF NORMAL SEMEN

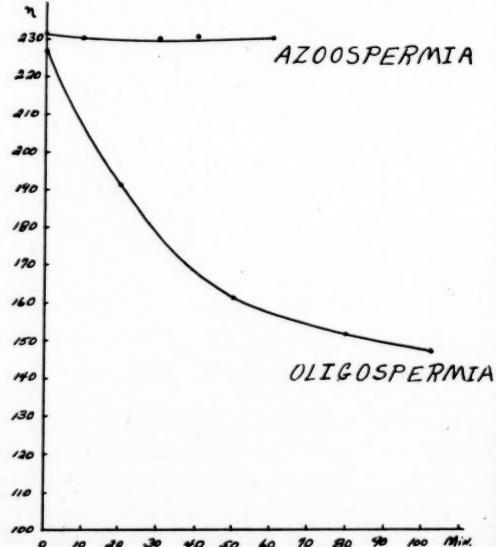
- The corrected time is "a plus half of b"—for reduction of the viscosity from the moment of contact of the semen and substrate
- The time of flow for distilled water is estimated in a control experiment
- The time of flow of solution of the substrate is another control
- The real viscosity equals b/d

The control values (d and e) are known from the preceding standardization of the substrate. It is safer to set up these control tests simultaneously with the semen analysis.

Viscosity of any material is subject to variations with the temperature, the pH and the concentration of electrolytes. It is best to perform the test at 20°C, at a pH of 4.8 and to use an exact 0.85 per cent solution of saline as diluting medium for the substrate.

The result of studies is evident from graphs. The amount of hyaluronidase decreases with the number of spermatozoa. In azoospermia, that is in semen without spermatozoa, and in aspermia resulting from obstruction of the seminal passages there is no hyaluronidase in the ejaculate.

Many a question has not yet been answered. Normally, hyaluronidase is present both in the seminal fluid and in the spermatozoa; if the sample lacks spermatozoa the enzyme is absent from both constituents. Exceptions to these



Graph II: VISCOSITY OF SUBNORMAL SEMEN

rules are encountered. Occasionally, the amount of enzyme and the number of cells do not conform. Studies of hyaluronidase content of semen after various types of treatment have not yet been summarized.

Therapeutic experiences with hyaluronidase are still limited. Identity of the enzyme in human and animal semen has not been definitely established. This question is important in view of the need for isolation of hyaluronidase needed as control in practical assays, in research, and for therapeutic purposes as well.

SUMMARY

A brief review of theories and facts about hyaluronidase is given.

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A SKIN TEST TO MEASURE SUSCEPTIBILITY TO WHOOPING COUGH

Preliminary Report

GEORGE J. BOINES M. D.*

Wilmington, Del.

The objective in the prevention of whooping cough cannot be attained, regardless of the seductive theories of routine immunization injections of various pertussis antigens and combinations thereof, or the recognized medical abilities of the physician, unless the parents of the young patients can be assured that the immunization will develop the desired protection against whooping cough.

It is definitely established that deficiencies in immunity against diphtheria can be determined by the easily performed Schick test, and in the case of scarlet fever by the Dick test. The need for a simple and easily performed skin test to measure the immunity index of pertussis requires no elaboration. The lack of such a test no doubt accounts for the paucity of authentic data about pertussis immunity in general.

A variety of tests for assessing immunologic response following pertussis vaccine injections have been reported, but these require laboratory facilities and specialized technique. Daughtry-Denmark¹ used complement fixa-

tion and agglutination reactions; Mishulow et al.² expressed a preference for the mouse protection test as an index of immunity.

Flosdorff et al.³ described a new skin test for whooping cough, using a purified agglutinogen, which, in their hands distinguished susceptible persons from the immune.

Stream et al.⁴ described a skin test with purified pertussis toxin, in which an immune response is obtained in only those who have recovered from the disease or those immunized with toxoid. A repetition of Stream's work by Silverthorne and his associates⁵ has shown that the toxin does not distinguish between those who have had the disease and those who are presumably susceptible.

Following a comparative study of pertussis agglutinogen skin test and complement fixation test, Sauer and Markley⁶ concluded that "the agglutinogen skin test seems to be a simple method by which persons who are immune to pertussis can be readily differentiated from those nonimmune."

Factors Influencing Skin Reaction. The immunologic diagnostic test is manifested by two types of dermal allergy. One depends on the presence of circulating antibodies, resulting in a response in about 15 minutes after the inoculation of the antigen, and usually disappears in three hours. The other type is always of a delayed nature, being a true tissue allergy, in which there is no reaction for a number of hours following the injection of the antigen. The maximum intensity of the reaction is reached after 24 hours, being manifested by induration, pain and redness.

It is thus assumed that if antibody is present in the blood stream and thereby presumably in the tissues, the injected antigen will excite an inflammatory reaction indicating the presence of protective substances. There is analogy with the tuberculin test rather than with the Schick test.

Agglutinogen for Pertussis Skin Test. The reports of Flosdorff and Kimball⁷, Felton and Flosdorff⁸, and Smolens and Mudd⁹ have established agglutinogens from phase I of *Hemophilus pertussis* as the specific fraction for the pertussis skin test to differentiate between the immune and nonimmune.

Impressed by these reports, it was decided to try a purified agglutinogen* in three groups of children.

Procedure and Interpretation of Skin Test.

* Physician in Communicable Diseases, Doris Memorial Hospital Unit, Wilmington General Hospital.

One-tenth cc. of the agglutinogen was injected intradermally and readings of the skin reactions made 30 minutes and 24 hours after injection.

As has been indicated, two types of dermal responses were anticipated; an immediate, or wheal-like reaction, and a delayed or tuberculin-like reaction. Induration is the determinant factor in a positive immune reaction to distinguish it from a negative reaction. Erythema alone is not considered in the interpretation.

The following procedure for grading reactions has been suggested:

1. Positive Immune—An indurated reaction (with or without erythema) 20 mm. or more in diameter at either one-half or 24 hours or both.
2. Weakly Positive Immune—An indurated area (with or without erythema) not exceeding 20 mm. in diameter at either one-half hour or 24 hours, but at least 10 mm. in diameter at either or both.
3. Negative Susceptible—No induration at either one-half hour or 24 hours beyond an area 10 mm. diameter.

All reactions will fade quickly, usually disappearing in 36 hours or sooner.

Results. A tabulation of the results is given with necessary details of explanations:

Group	Number Tested	Ave. Age	H. Pertussis Skin Test			
			Vaccine Injections	P.I.	W.P.I.	N.S.
I-A	16	10.2 Months	None	0	2	14
I-B	6	8.8 Years	None	0	0	6
II	5	6.9 Years	None	5	0	0
III	32	5.5 Years	Yes	22	5	5

P. I.—Positive Immune.

W. P. I.—Weakly Positive Immune.

N. S.—Negative Susceptible.

Group IA consisted of 16 patients ranging from 3 months of age to 42 months of age with an average of 10.2 months. None of these patients had received injections of H. pertussis vaccine. Fourteen of these were negative susceptible and 2 were weakly positive immune.

Group IB with 6 patients ranging from 5½ years to 14 years with an average of 8.8 years who had not been injected with H. pertussis vaccine at any time. All of these patients were, according to the skin test, negative susceptible.

* Supplied through the courtesy of Steven Horoschak of the Medical Research Division of The National Drug Company, Philadelphia, Penna.

Group II. Five patients in this group from 5½ years to 10 years of age with an average of 6.9 years. All of these patients had had whooping cough disease from 2 years to 8 years—average of 4.4 years prior to skin testing. Four of the patients were strongly positive immune and one was just over the borderline.

Group III. The 32 patients in this group had received injections of H. pertussis vaccine. The patients ranged from 17 months of age to 9 years of age.

Twenty of this group had been injected with H. pertussis vaccine within 3 years of the skin test, all being positive immune. Two of the patients had been given vaccine 4½ and 7½ years prior to test, being positive immune.

Five patients given H. pertussis vaccine 3 to 6½ years previously, tested weakly positive immune.

Three patients injected with H. pertussis vaccine from 15 months to 3½ years previously were negative susceptible.

Two patients were negative susceptible 4 to 4½ years following injection of H. pertussis vaccine.

COMMENTS

The observations made in the course of this study tend to indicate that a purified agglutinogen should prove effective and satisfactory for determining the immunity index for whooping cough. The pertussis skin test is simple and easily performed and the interpretations of the test are not difficult.

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W. EDWIN BIRD, M. D. Editor
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C. LEITH MUNSON, M. D. Associate Editor
1005 Jefferson Street
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No. 2

MUCH NEEDED INFORMATION

The Council on Medical Service of the American Medical Association is to be congratulated on the excellence of its newly issued compilation "Voluntary Health Insurance vs. Compulsory Sickness Insurance." The booklet of 124 pages contains twenty-four articles from various sources and an introduction by Edward J. McCormick, M. D., Chairman of the Council, and constitutes a handy reference work for writers, speakers, and debaters, as well as for the information of the doctors and the public in general. We quote from the introduction:

If the answer to whatever medical problems may exist cannot be given by the 90 per cent of physicians whose opinions are generalized in this work, there can be no logical answer. We expect engineers, lawyers, ministers, and architects to guide us when national problems in their respective fields confront the Nation. We follow our great military and naval leaders when our country is threatened by other

nations. This is as it should be. Trained men should guide us in their particular fields. Who would desire to have his house built by a doctor or lawyer? Who would choose as his architect a soldier or minister? Who would feel safe in a court of law represented by a social worker, a politician, or an engineer?

The medical profession is opposed to communism, socialism, collectivism, and compulsion in any field of endeavor in America and especially in the medical field. There is no selfishness in our stand. We desire better living conditions and increased opportunity for all. We recognize the fact that medical progress must cease and that sickness and mortality will increase under any government program of compulsory health insurance. We do not desire the promised increase in medical incomes under government control.

It is the hope of the Council on Medical Service of the American Medical Association that the material herein assembled will give to those who peruse it a few of the reasons for the desire of all physicians to remain free men and free women. As we have contributed during war and disaster, so we now desire to contribute in peace to the welfare of all and to the preservation of Democracy.

We hope that this booklet will be read thoroughly by doctors and the public alike. The importance of the subject is great. Sooner or later the public will have to decide which path it will travel. The final decision should be based on the fullest possible information—not propaganda. Therefore, such a compilation of source material from widely scattered publications, all authoritative, and issuing from a responsible Council of the American Medical Association is a valuable step in the right direction.

Along the same lines, the Medical Society of the State of New York, through its Bureau of Public Relations, has prepared and will shortly issue a handbook in the form of questions and answers on the subject of sickness insurance, entitled "Check and Double Check," by Mr. J. Weston Walsh, a school teacher of Portland, Maine. Mr. Walsh discusses the question of voluntary health insur-

ance vs. compulsory sickness insurance, giving what he thinks are the outstanding points in the controversy, from the standpoint of a plain American citizen, just as they impressed him in the course of his own work on the handbook.

Mr. Walsh was asked to do the job because this question will ultimately be decided in the forum of public opinion. He is thinking here of what would happen to *him* under compulsory sickness insurance. As an average citizen, he does not like it. Legislators already know the doctors do not like it. Here is the evidence that the J. Weston Walshes of the country do not like it either.

It is hoped this subject will be approached in the spirit of inquiry, which is Mr. Walsh's attitude, before opinions are formed on so important a matter as how to obtain medical care. Hence, the title, "Check and Double Check."

Free of large masses of statistics, and written in a colloquial style, the author's aim is simplification without distortion. This painstaking work is offered for use as a speaker's handbook. For this purpose, a ready-reference index is provided. The pamphlet is intended for editorial writers, radio commentators, ministers, teachers, lawyers, and members of Chambers of Commerce, Parent-Teachers' Associations, Women's Clubs, labor unions and Granges, as well as doctors called upon to speak on the subject.

Copies of the American Medical Association's pamphlet may be had by writing to the Council on Medical Service, American Medical Association, 535 North Dearborn Street, Chicago 10, Illinois.

Those desiring copies of "Check and Double Check," may obtain them by writing to the Bureau of Public Relations, Medical Society of the State of New York, 292 Madison Avenue, New York 17, New York.

N. Y. St. J. M., Jan. 1, 1947.

MISCELLANEOUS Voluntary Health Plans

"Driving to complete the voluntary health insurance program for the care of the American people is the big job facing local, state and national medical organizations today," according to Thomas A. Hendricks, secretary

of the Council on Medical Service of the American Medical Association. "More than 80 plans sponsored by medical societies in 33 states covering 4,000,000 persons are now in operation and the task has just begun.

"The pioneering state of voluntary health insurance is nearing completion and, nationally, we are rapidly entering the development stage. Only two states do not have a plan operating or in the process of formation. Plans for a prepayment program are now being made in 13 states and the District of Columbia. Growth of the plans now in operation has been rapid, the over-all expansion within the last six months being as phenomenal a production figure as has appeared in modern insurance records.

"The enrollment in prepayment plans has accelerated slowly. This was partly due to the difficulties developed in the early experimentation stages through which such plans had to pass, and partly to hesitancy on the part of doctors to plunge into an untested field of endeavor. As the number of plans has increased, so too has the acceleration in enrollment. During 1945 the over-all increase was 114 per cent. For the first six months of 1946 the enrollment increase was approximately 40 per cent, bringing the total to nearly the 4,000,000 mark. Indications are that enrollment will reach 5,000,000 by early 1947.

"One of the objectives of the Council on Medical Service is to present the facts in regard to advantages and disadvantages of the various plans, keep records up to date on all new developments in the medical care field, conciliate differences of opinion as to the various forms of insurance—in short, view the entire question impartially and objectively, in order to do everything possible to encourage the wholehearted acceptance by every state society of a practical, workable plan.

"The whole insurance program is still experimental. No one knows the complete answer. Hence, the council hopes to encourage all types of plans that meet the minimum requirements set by the council to maintain the standard of medical service for the protection of the public.

"The council is now set up to do the job of (1) encouraging development of new plans; (2) keeping the profession informed as to de-

velopments, and (3) helping to increase the enrollment of plans already established.

"A prepayment division of the council has been created with George Cooley, assistant secretary of the council, keeping in contact with medical society-sponsored plans; Howard Brower, maintaining contact with private insurance groups; and L. S. Kleinschmidt, concentrating his efforts on encouraging rural enrollment and maintaining contact with the newly created consumer-cooperative movement.

"Prepayment plans have progressed rapidly in the cities, but development in the rural areas has been slow, although several plans have been making notable advancements along this line.

"Jay Ketchum, Lansing, executive vice president of Michigan Medical Service, is acting as consultant for the council.

"Within the past few months private insurance carriers are showing an intense interest in medical and surgical care coverage and, as a result, there have been many conferences both formal and informal. A joint conference was held with representatives of large insurance associations in Chicago in September, with Dr. E. J. McCormick, of Toledo, chairman of the council, presiding.

"One of the most important developments has been the creation of Associated Medical Care Plans, with Dr. H. L. Schriver, of Cincinnati, O., as president; William M. Bowman, San Francisco, vice president; Jay Ketchum, secretary; and Dr. Norman Scott, Newark, N. J., treasurer. In a sense this is a trade organization of plans. It can be of great service in developing reciprocity, details of selling, cooperative actions and procedures. Frank Smith, who has served with the California Physicians' Service, San Francisco, as director of public relations, recently has been appointed A. M. C. P. director. Although A. M. C. P. will be housed with the council and its work integrated with the work of the council and in accord with the policies of the council, it is a legal entity separate and distinct from the council. The board of trustees has allotted through the council sufficient funds to this organization to get started.

"The council is also aided by Frank Dickinson, Ph. D., director of the Bureau of Medical

Economic Research of the American Medical Association, and T. V. McDavitt of the A.M.A. staff has served as the legal advisor of A. M. C. P."

Veterans Administration Adopts Artificial Eye Developed By Army

The Army's plastic artificial eye has been used by more than 7,500 former soldiers during the past three years and has been adopted by Veterans Administration in furnishing ocular prostheses to patients, the War Department announced recently.

Developed first in 1943 by a former major in the Army Dental Corps while stationed in England, this type of acrylic eye has practically replaced glass eyes which were used almost exclusively before World War II. The Army Medical Department developed this eye after the war broke out, when both civilian and military supplies of artificial eyes were depleted due to high breakage and inability to replenish supplies. Glass eyes then used in the United States were largely German-made.

As early as 1943, the Army made plans to discard the easily breakable, inferior, custom-made glass eye when Major, (then Lieutenant) Stanley F. Erpf of San Francisco, California, assigned to the job by Col. Derrick T. Vail, Consultant in Ophthalmology in ETO, successfully demonstrated the artificial eye made of water-clear plastic and individually fitted and colored. In January 1944 the first training center for ophthalmoprosthetists was organized at the 30th General Hospital, England. Forty American dental officers and 10 British dental officers attended.

Dr. Robert E. Stewart, Chief of the Ophthalmoprosthetic and Restoration Division of The Prosthetic Appliances Service of Veterans Administration, said today that all 15 technicians making artificial plastic eyes for VA are Army-trained. They were dental officers and technicians especially trained in this work during the war.

"The Army-developed artificial eye has proven superior to any other type of ocular prosthesis available today," Dr. Stewart declared. "Of about 500 World War II veterans who have applied to Veterans Administration for ocular prosthesis aid, none had any

serious complaint about the acrylic eye. They wanted lost eyes replaced, socket corrections or needed re-fitting because of other operations."

Dr. Stewart said the Army-developed eyes were never broken when dropped nor has the coloring in the eyes deteriorated. He explained that some eyes had become roughened due to hard usage, but this is easily remedied.

Veterans Administration scientists have changed the Army's painting technique slightly in making the eyes, but that is the only difference in government-issue and V A artificial eyes. Some scientific circles were of the opinion that the nylon threads used in veining the eyes would deteriorate and lose their original color. Dr. Stewart reported that no such deterioration has been noted by V A specialists.

Another principal feature of the durability of Army-founded artificial eyes is that there is no evidence of etching or corrosion even in eyes worn by patients over a three-year period.

Credit for the development of the Army's acrylic eye is accorded by Major General Norman T. Kirk, The Surgeon General, to Major Erpf, who initially introduced the eye which has undergone few modifications. He returned to the United States from England in June of 1944 to collaborate with Major Milton S. Wirtz, Latimer, Iowa, and Major Victor H. Dietz, Chicago, Illinois, ocular prosthetic specialists in perfecting the acrylic eye, at Valley Forge General Hospital, Phoenixville, Pennsylvania. A school was started here to train technicians who were then sent to other general hospitals.

By that time, 13 general hospitals in the European Theater of Operations possessed personnel and facilities for the fabrication of acrylic eyes. In October, 1944, 12 general hospitals in the United States were similarly equipped. The Army continued to enlarge upon its artificial eye program until in October, 1945, 30 Medical Department installations have inserted more than 7,500 plastic artificial eyes. When V-J Day came there were acrylic eye teams in Hawaii and the Philippines.

General Kirk said that Army patients equipped with this prosthesis were issued new eyes whenever medically necessary. No re-

quests were received for replacement of the eye because of structural or material weakness. Veterans Administration reports the same findings among veterans wearing this acrylic eye.

News Notes, Jan. 15, 1947.

Venous Thrombosis

Venous thrombosis, a condition in which the blood clots in the veins, is of two types—thrombophlebitis and phlebothrombosis, according to Alton Ochsner, M. D., of New Orleans. He states that unless there is a differentiation between the two, treatment is "likely to continue to be unsatisfactory."

Writing in the December 7 issue of *The Journal of the American Medical Association*, Dr. Ochsner points out this difference: the blood clot in thrombophlebitis is the result of inflammatory changes and is firmly attached to the vein wall; the blood clot in phlebothrombosis is the result of tissue injury and can become detached easily from the vein wall.

Thrombophlebitis usually can be diagnosed easily from symptoms such as fever, pain and swelling. The patient's chances of recovery are good, but, if he does not receive effective treatment, complications such as swelling, pain, ulceration of the legs and infection may develop.

In contrast, patients with phlebothrombosis, although apparently not ill, are potential fatalities because of the danger that the clot will become detached and be carried by the blood stream to the lungs where it may act as a plug and cause death.

Phlebothrombosis is caused by two things—an increase in the ability of the blood to clot due to tissue injury and a slowing of the flow of blood as a result of the patient's being confined to bed or having a leg in a cast. Early detection of this condition is possible if the patient is examined for tenderness of the legs following any tissue damage such as an operation.

Dr. Ochsner states that "there is a definite relationship between venous thrombosis and the seasons." This has been pointed out by several other investigators. One of these found the greatest incidence of thrombosis from December to February. He believes

that grippal infections are responsible for this difference.

Another group of investigators reported that in a series of 332 cases thrombosis was observed in 32.9 per cent in the winter, 21.9 per cent in the spring, 18.9 per cent in the summer and 20.3 per cent in the fall.

"It is my belief that the increased incidence of venous thrombosis during the winter months is due to the vasospastic influence of the cold weather," states the author. "This explains the difference between the incidence of venous thrombosis observed in the northern and in the southern clinics. My associates and I showed that the incidence of venous thrombosis in the northern clinics was almost double that in the southern clinics. The average incidence in the northern states was 0.74 per hundred thousand population as contrasted with 0.41 in the southern states."

Several suggestions are made by Dr. Oehsner which, if followed, he believes should prevent the formation of clots in the veins. He says that patients should refrain from smoking for a period of from 10 to 14 days before an operation; overweight patients should reduce before undergoing surgery; any abnormal state of the blood, such as anemia, should be corrected. After the operation the author favors leg exercises and deep breathing to increase the circulation.

For the treatment of thrombophlebitis the author suggests the use of a local anesthetic, procaine hydrochloride. "The pain is relieved instantly, the temperature falls rapidly and the swelling subsides within a few days," he writes. "My experience has shown that the relief of pain is complete and permanent in 90 per cent of the patients, whereas in 10 per cent a second block [of the local involuntary nerve centers] is necessary to give permanent relief."

Dr. Oehsner recommends immediate surgery as soon as phlebothrombosis has been diagnosed. He does not favor widespread use of anticoagulants such as heparin and dicumarol because, although they will prevent further clotting of the blood, they will not prevent the detachment of the clots already formed.

Streptomycin in Pylephlebitis

The new antibiotic drug—streptomycin—which comes from a group of living organisms found in garden soils, river muds, peats and compost heaps has proved effective in the treatment of pylephlebitis, a usually fatal disease.

Two Minneapolis physicians, writing in the February 22 issue of *The Journal of the American Medical Association*, state that they used the drug in treating a case of pylephlebitis and the patient's recovery was dramatic. Pylephlebitis, which is an inflammation on the inside of the principal vein of the liver, is often a complication of a gangrenous appendix. Data on cases of the disease with multiple abscesses of the liver show an exceedingly high mortality rate.

Drs. J. H. Wishart and L. J. Peterson, who are from the Veterans Administration Hospital, Minneapolis, and the Departments of Medicine and Surgery, University of Minnesota, report that in one series of 68,198 cases of appendicitis there were 247 cases complicated by multiple abscesses of the liver, an incidence of 0.36 per cent. Another investigator reported 1,463 cases of appendicitis with 12 cases of pylephlebitis.

Drs. Wishart and Peterson say that in 1938 two cases were treated with sulfanilamide with subsequent recovery; in another case sulfathiazole treatment resulted in cure and in 1945 a case was treated with penicillin and the patient recovered completely.

The two Minneapolis physicians used streptomycin in treating a 28-year-old man who was admitted to the hospital with generalized cramping abdominal pain, recurrent chills and fever and headache. A diagnosis of acute appendicitis was made and the patient was operated on two hours later. The man's condition remained unchanged after the operation. His fever remained high and he suffered recurring chills. Penicillin treatment was started a day after the operation, but was discontinued after the fourth day because there was no great improvement in the patient's condition.

The postoperative clinical course and laboratory observations resulted in a diagnosis of pylethrombophlebitis. The patient was placed on streptomycin therapy immediately. At the

start, he was given the drug every six hours.

There was a gradual improvement in his condition, the doctors say, adding that "at no time while on streptomycin therapy did he receive any other medicament that in any way could confuse the results obtained by streptomycin therapy."

Cold Anesthesia For Surgery

"Experience to date continues to confirm the safety and benefit of refrigeration anesthesia," according to Drs. Lyman Weeks Crossman and Frederick M. Allen of New York, who first demonstrated the advantages of this type of anesthesia.

Writing in the February 8 issue of *The Journal of the American Medical Association*, the physicians, who are from City College, Welfare Island, state that the "trial period of surgical refrigeration may be measured from the first publication of experiments on animals and clinical cases in 1937 or, better, from the adoption of the method on the surgical service of the City Hospital in 1941."

Experiments have demonstrated that cold serves as a shockless anesthetic in surgery, preserves injured tissue and restrains infection until the patient is strong enough to undergo an operation. Moreover, it reduces pain and swelling.

Drs. Crossman and Allen point out that "in cases of severe trauma of limbs, refrigeration serves preeminently to gain time in an emergency by preserving the injured part for days or weeks until the patient gains sufficient constitutional strength to withstand amputation. A secondary benefit, however, is reported as the development of collateral [secondary] circulation during the time thus gained, so as to permit a lower level of amputation. This may make the difference between an emergency amputation high in the thigh and an amputation just above the knee a few weeks later. . . . This difference has practical importance for the patient's subsequent walking and earning ability."

The authors recall that the "first observations along the line of preservation of infected or injured parts were made when patients entered our hospital with acutely dangerous infected gangrene, but legal permission for the necessary amputation could not be imme-

diate obtained. We thus learned that packing such limbs in ice or ice bags made possible not only a safe postponement of the operation for several days but even an improvement in the general condition so as to lessen the operative risk. . . .

"A more definite preservation may be attempted in treatment of other infections of the limbs, such as gas gangrene. Refrigeration is helpful even when amputation is inevitable, but in less extreme conditions the radical chilling contributes to save the limb in two ways: by directly checking the toxin [poison] production and its necrotizing action on the tissues and by gaining time for administration of drugs or other systemic means of cure. A tourniquet is not employed except as a preliminary to amputation."

Dr. Crossman cites a previous report of his in which he illustrates how refrigeration aids minor surgery in "restoring fingers which have been cut off so as to hang by a mere shred of skin. Such a finger may be kept well chilled according to instructions given by telephone and will thus remain viable [living] at least during several hours which may elapse before the patient can reach the doctor. Theoretically the interval might extend to 24 hours or more, though there is no clinical proof of such a maximum. After the finger is sutured in place the reduced temperature is still continued for several days but is raised slightly day by day as the nutrition of the severed part improves."

A. C. S. Meets in Baltimore

The first of a series of seven Sectional Meetings of the American College of Surgeons will be held in Baltimore on March 10 and 11, with headquarters at the Lord Baltimore Hotel, according to an announcement by Dr. Irvin Abell of Louisville, President and Chairman of the Board of Regents. Maryland, the District of Columbia, and surrounding states will participate. The other six Sectional Meetings will be held in Omaha, March 14-15; Fort Worth, March 20-21; Providence, March 28-29; San Francisco, April 7-8; Vancouver, April 21-22; and Winnipeg, April 28-29.

The medical profession at large, medical students, and hospital personnel, are invited to join with the Fellows of the College in the

meetings which will be addressed by nationally prominent visiting and local speakers.

The Sectional Meeting will open at 8:30 both mornings with the showing of medical motion pictures. On the first morning these will be followed at 10:00 o'clock by a scientific session for the medical profession on "Carcinoma of the Stomach," "Advances in Anesthesia," "Surgery of the Kidney," and "Surgery of the Thyroid in Relation to the Use of Thiouracil." At the same hour hospital personnel will open a symposium on five major postwar hospital problems.

Luncheons will be held on both days followed by round table conferences on subjects presented at the preceding morning sessions. The panel discussions for medical personnel on the first afternoon will be on "Intestinal Obstruction" and "Fractures." At a concurrent meeting, hospital personnel will discuss the management of emergency patients. On the first evening a dinner for Fellows, other members of the medical profession, and hospital representatives will be held, following which there will be talks on activities of the College, a premiere showing of a medical motion picture now under production, and a reception.

On the second morning, following the showing of medical motion pictures, the medical program will be devoted to discussion of "The Use of Antibiotics in Surgical Practice," "Surgery of Malignant Growths of the Neck," and "The Prevention of Pulmonary Embolism." The hospital personnel will hold a symposium on "Basic Considerations in an Efficient Personnel Management Program." Panel discussions on "Postoperative Care" and "Carcinoma of the Colon" will feature the afternoon medical program, while the hospital personnel will hold a round table conference on questions arising out of the three previous sessions and other problems not included in the program.

Blood Vessel Diseases

Two Veterans Administration physicians from the Wadsworth General Hospital in California, writing in the March 1 issue of *The Journal of the American Medical Association*, report a new method for the relief of patients suffering blood vessel diseases of the arms and legs with gangrene.

The method, it is reported, not only relieved the "intractable pain," but also cleared the gangrenous condition and, in some cases, prevented possible amputation.

The treatment is described in *The Journal* by Drs. Zolton T. Wirtschafter and Rudolph Widmann, who are from the Department of Medicine, Wadsworth General Hospital, Veterans Administration Center, Los Angeles. Physicians cooperating in the work included Roger O. Egeberg, chief of the medical service, Wadsworth General Hospital; B. O. Raulston, dean of the University of Southern California Medical School, and William H. Leake and Edmund R. Ware of the University of Southern California and Wadsworth General Hospital.

The new method consists of injecting into the patient's vein a substance called sodium ascorbate, which is related to vitamin C. This is followed by the intramuscular injection of a solution known as histidine monohydrochloride with the simultaneous injection under the skin of additional sodium ascorbate. The two organic compounds—sodium ascorbate and histidine monohydrochloride—are given every four, six, eight or 12 hours, depending on the severity of the patient's condition. In addition, all patients are given ascorbic acid or vitamin C by mouth each day.

It is believed that the body's reaction is a transformation of the histidine into histamine by the action of the ascorbic acid within the body.

This new method of treatment causes the body to produce histamine, classified as a chemical substance, which is known to cause a relaxation of the blood vessels and an increase of blood flowing through them. The authors believe it is the first time that this technique has been tried to produce histamine itself in

the patient's own body for the purpose of treating disease.

Drs. Wirtschafter and Widmann tried their treatment on 11 patients suffering from various forms of blood vessel disease. Four of the patients were suffering from gangrene and in one of them diabetic gangrene involved the fourth right toe.

In reporting the results, the doctors say: "All of these patients have up to the date of this report responded favorably to the therapy described and have not required amputations. The relief of intractable pain has been dramatic in the persons afflicted with it. The relief has occurred within six hours to three days after the institution of treatment. Patients with gangrene, regardless of the cause, have described a sensation of increased warmth in the affected limbs. . . .

"Extremities exhibiting black, shriveled, hard, mummified toes have shown areas of rubor (color) in the affected parts 48 hours after the institution of therapy."

The doctors explain further that in all cases exhibiting gangrene, there was a gradual return of function of the extremities although sensation was slow in returning.

In two instances of a certain type of blood vessel disease "the response was rapid," the doctors state, adding: "The relief of pain, the sensation of warmth and an increase in temperature of the affected extremities were again observed."

The physicians say their technique is now being investigated for the treatment of many other diseases in which circulation has failed, including coronary artery disease, angina pectoris and hypertension, and other conditions related to a deficiency of histamine.

Prize Contest

The American Association of Obstetricians, Gynecologists and Abdominal Surgeons announces a foundation prize contest.

For further information write Dr. James R. Bloss, Secretary, 418 Eleventh Street, Huntington 1, West Virginia.

Correction

In the article entitled "Penicillin Treatment of Pneumococcic Meningitis" by George J. Boines, M. D., in THE JOURNAL of February, 1946, page 37, paragraph 1, line 10 appears the word "thoracocentesis." This should have read "rachicentesis."

BOOK REVIEW

Allergy in theory and practice. By Robert A. Cooke, M. D. Attending Physician and Director of the Department of Allergy, the Roosevelt Hospital, New York City. Pp. 572, with 43 illustrations. Cloth: price, \$8.00 Philadelphia: W. B. Saunders Company, 1947.

The book is most complete and practical, and is written in a fascinating style. It is divided into nine sections, including an appendix. The opening section deals with the principles and theory of allergy, as well as the pathological and immunological aspects. The following sections then deal with the various types of allergy including asthma, hay fever, allergies of the skin, nervous system, cardiovascular system, digestive system, and the eye. Particularly illuminating are the special articles on allergic neuropathies including migraine, Meniere's Disease, and histamine cephalgia. Also, there is an interesting chapter on allergy in infancy and childhood. Section 8 deals with the bacterial allergies, as well as the inhalants, foods, drugs, endocrine, serum, and physical allergies. These chapters are most complete and bring one up to date with the causative factors. The final chapter in Section 9 deals with the opinion as to the value of the different techniques, as to skin testing, and finally, laboratory procedures, including the methods by which the various antigens are prepared. The appendix deals with the non-specific causes, as psychic, nutritional, and endocrine factors in relation to allergy.

This book is most readable, practical, up-to-date, and certainly can be recommended to the general practitioner for references, as well as to the specialist in the allergic field.

